

In the Specification

On page 1, kindly insert the following paragraph immediately following the title:

--Cross Reference to Related Applications

This application is the U.S. national phase of International Application No. PCT/GB2003/003747 filed on August 29, 2003 and published in English on March 11, 2004 as International Publication No. WO 2004/019980 A1, which application claims priority to Great Britain Application No. 0220257.0 filed on August 31, 2002, the contents of which are incorporated by reference herein.—

On pages 10 and 11, kindly amend the paragraphs beginning at line 21 as follows:

F1 is expressed optimally at 37°C and is thought to inhibit phagocytosis through the formation of a capsule-like structure on the bacterial surface, and is an effective plague vaccine (Andrews, G. P. et al. 1996. *Infection and Immunity* 64:2180-2187; Du, Y. D. et al. 2002. *Infection and Immunity* 70:1453-1460; Heath, D. G. et al. 1998. *Vaccine* 16:1131-1137; Titball, R. W. et al. 1997. *Infection and Immunity* 65:1926-1930). A recent report showed that an isogenic F1 plague mutant has impaired resistance to phagocytosis by J774 cells (Du, Y. D. et al. 2002. *Infection and Immunity* 70:1453-1460). Also, a virulence plasmid cured strain, deficient for TTS, was less resistant to phagocytosis and an additive effect was seen with the double mutant (F1-negative, plasmid cured strain). It was proposed that the TTS system and F1 capsule synthesis contribute in different ways to maintain the extracellular lifestyle of *Y. pestis* (Du, Y. D. et al. 2002. *Infection and Immunity* 70:1453-1460). By using the invention, both the TTS system and the F1 capsule of the organism are targeted, which might explain the high level of protection observed in the following examples. The present invention will now be described only by way of examples in which reference shall be made to the following Figures in which:

~~Figure 1 is a graph showing therapeutic Mab 7.3 treatment of mice challenged with *Y. pestis* via the s.c. (A) and aerosol (B) infection routes. Mice received 35 µg of Mab 7.3 in PBS by i.p. injection 4 hours before or up to 72 hours after challenge, as indicated. Deaths were recorded over a 14 day period. Delayed time to death observed in animals treated with Mab 7.3 at 72 hours (A) and 60 h (B) were statistically significant ($P < 0.05$) by Student's T-test analysis compared with untreated control groups~~

~~Figure 2 is a graph showing that Mab 7.3 and FI-04-AG-1 display synergy when administered post-infection. Mice were challenged s.c. with 91 MLD *Y. pestis* and treated 48 hours after plague challenge with Mab 7.3 (35 µg), FI-04-A-G1 (100 µg) or both antibodies. Deaths were recorded over a 14 day period.~~

On page 14, kindly amend the first complete paragraph as follows:

Mab 7.3 was administered -4 hours, +24 hours, +48 hours, or +96 hours relative to s.c. *Y. pestis* challenge. Protection was observed when antibody was given up to 48 hours post-infection (Fig. 1A). Also, a delayed time to death was observed in the +96 hours treatment group. One of +96 hours treatment group had died prior to antibody administration and the remainder displayed signs of plague indistinguishable from untreated control animals, suggesting that even when symptoms of plague are apparent antibody therapy can delay death. Mice were treated with Mab 7.3 at -4 hours, +24 hours, +48 hours or +60 hours relative to aerosol infection (Fig. 1B). Protection was seen in groups that received antibody 24 hours and 48 hours after challenge. All mice treated at +60 hours died, but a statistically significant delay in the TTD was observed, compared with untreated animals.

On page 15, kindly amend the first complete paragraph as follows:

This confirmed the prophylactic properties of FI-04-A-G1 in the pneumonic plague model (Anderson, G. W. et al. 1997. American Journal of Tropical Medicine and Hygiene 56:471-473). Mab 7.3 was less effective as a treatment against s.c. *Y. pestis*

challenge than aerosol challenge (Fig. 1), therefore the bubonic plague model chosen for further co-administration studies to test for antibody synergy.

On page 15, kindly amend the paragraph beginning at line 25 as follows:

Surprisingly, protection was observed at all challenge doses; breakthrough was expected at challenge doses greater than 100 MLD (see Table 1 and Anderson, G. W. et al. 1997. American Journal of Tropical Medicine and Hygiene 56:471-473). Next the combined antibody treatment was tested as a plague therapy. Mice that received the antibody cocktail 48 hours after challenge were protected better than animals that received single antibody therapy (Fig. 2). The data indicates that Mab 7.3 and F1-04-AG1 act synergistically as a pre-treatment and as a therapeutic in our plague models.